

## ZINC FINGER PROTEIN DERIVATIVES AND METHODS THEREFOR

### ABSTRACT

5 Zinc finger proteins of the Cys<sub>2</sub>His<sub>2</sub> type represent a class of malleable DNA binding proteins which may be selected to bind diverse sequences. Typically, zinc finger proteins containing three zinc finger domains, like the murine transcription factor Zif268 and the human transcription factor Sp1, bind nine contiguous base pairs (bp). To create a class of proteins which would be generally applicable to target unique sites within complex genomes, the present invention provides a polypeptide linker that fuses two 10 three-finger proteins. Two six-fingered proteins were created and demonstrated to bind 18 contiguous bp of DNA in a sequence specific fashion. Expression of these proteins as fusions to activation or repression domains allows transcription to be specifically up or down modulated within cells. Polydactyl zinc finger proteins are broadly applicable as genome-specific transcriptional switches in gene therapy strategies and the 15 development of novel transgenic plants and animals. Such proteins are useful for inhibiting, activating or enhancing gene expression from a zinc finger-nucleotide binding motif containing promoter or other transcriptional control element, as well as a structural gene or RNA sequence.

LJ-32257-1